

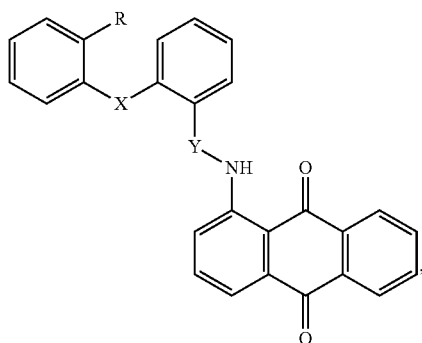
## SUMMARY

**[0009]** An embodiment of the invention relates to a method for restoring or preserving cholesterol efflux in a cell infected with Human Immunodeficiency Virus (HIV) comprising delivering to the cell an effective amount of a composition or formulation comprising a small molecule. The small molecule prevents or decreases an interaction between a Negative Regulatory Factor (Nef) protein and a Calnexin protein.

**[0010]** Another embodiment of the invention relates to a method for treating or preventing atherosclerosis in a subject infected with HIV comprising administering to said subject an effective amount of a composition or formulation comprising a small molecule. The small molecule prevents or decreases an interaction between a Nef protein and a Calnexin protein.

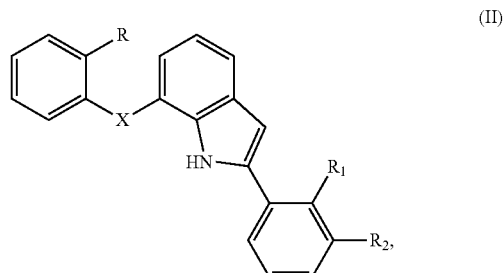
**[0011]** Another embodiment of the invention relates to a method for screening for a small molecule that restores or preserves cholesterol efflux in a cell by inhibiting or decreasing an interaction between a Nef protein and a Calnexin protein including: incubating a cell expressing a full-length Nef protein or a segment of the full-length Nef protein and a full-length Calnexin protein or a segment of the full-length Calnexin protein with a small molecule of interest; assaying the incubated cell for cholesterol efflux; and assaying the incubated cell for a level of binding between the full-length Nef protein or the segment of the full-length Nef protein and the full-length Calnexin protein or the segment of the full-length Calnexin protein. In such embodiments, an increase in cholesterol efflux and a decrease in the level of binding as compared to a control is indicative of restoration or preservation of cholesterol efflux by inhibiting or decreasing an interaction between the Nef protein and the Calnexin protein as a result of incubation of the cell with the small molecule of interest.

**[0012]** An embodiment of the invention relates to a small molecule having the structure of Formula (I):



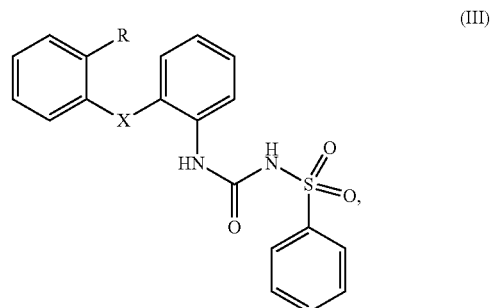
Where R is H, CH<sub>2</sub>OH, COOH or COOCH<sub>3</sub>; X is CH<sub>2</sub>, NH, O, NCH<sub>3</sub>, or SO<sub>2</sub>; and Y is a bond, CH<sub>2</sub>, CO or SO<sub>2</sub>.

**[0013]** An embodiment of the invention relates to a small molecule having the structure of Formula (II):



Where R, R<sub>1</sub>, and R<sub>2</sub> are independently selected from H, CH<sub>2</sub>OH, COOH or COOCH<sub>3</sub>; and X is CH<sub>2</sub>, NH, O, NCH<sub>3</sub>, or SO<sub>2</sub>.

**[0014]** An embodiment of the invention relates to a small molecule having the structure of Formula (III):



Where R is H, CH<sub>2</sub>OH, COOH or COOCH<sub>3</sub>; and X is CH<sub>2</sub>, NH, O, NCH<sub>3</sub>, or SO<sub>2</sub>.

## BRIEF DESCRIPTION OF THE DRAWINGS

**[0015]** Further objectives and advantages will become apparent from a consideration of the description, drawings, and examples.

**[0016]** FIG. 1A shows a schematic of HA-tagged full-length and mutant calnexin constructs expressed in HEK293T cells ("RKPRRE" is disclosed as SEQ ID NO: 1);

**[0017]** FIG. 1B is an immunoprecipitation assay showing expression of HA-tagged full-length and mutant calnexin constructs HEK293T cells;

**[0018]** FIG. 2A shows representative models of Nef-CNX binding;

**[0019]** FIG. 2B shows interactions in Nef-CNX docking models mapped on Nef and calnexin sequences;

**[0020]** FIG. 3A shows immunoprecipitation results comparing the interaction between Nef Wild Type and Calnexin and NefK4,7A and Calnexin;

**[0021]** FIG. 3B shows immunoprecipitation results comparing the interaction between Nef Wild Type and Calnexin and various Nef mutants and Calnexin;

**[0022]** FIG. 3C shows ABCA1 abundance as a function of mutations to Nef;

**[0023]** FIG. 3D shows NefK4,7A interaction with ABCA1 as compared to ABCA1 interaction with wild-type Nef;